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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	10/035,349	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-58 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-58 is/are rejected.

7)☒ Claim(s) 26 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Workgroup 1630, Art Unit 1634, and has been docketed to Primary Examiner Bradley L. Sisson.

Specification

2. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states at page 82: "All publications, patents, and patent applications cited herein are hereby incorporated by reference in their entirety for all purposes." Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly

> incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Attention is also directed to MPEP 608.01(p)I, which, in pertinent part, is reproduced below:

> Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found. (Emphasis added)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

3. The disclosure is objected to because of the following informalities:

a. At page 2, line 9, there appears an attorney docket number.

b. Page 24, line 32, makes reference to a US Patent application, but does not provide the current status of same.

Appropriate correction is required.

Claim Objections

4. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 26 depends from itself.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1-58 are indefinite with respect to what constitutes the metes and bounds of an "oligomer." Page 15 of the specification provides the following definition:

> As used herein, the term "oligomer" refers any polymer of residues wherein the residues are similar, though typically not identical. Generally, an oligomer is meant to include the naturally-occuring polymers such as proteins, oligonucleotides, nucleic acids, oligosaccharides, polysaccharides, and lipids, and the like. Oligomer may also refer to free radical, condensation, anionic, or cationic polymers of synthetic origin, such as but not limited to: acrylates, methacrylates, nylons, polyesters, polyimides, nitrile rubbers, polyolefins and block or random copolymers of different monomers in these classes of synthetic polymers. The oligomer that is subject to the analytical methods described herein will have a number of residues that is typical of their naturally occuring number. For example, an oligomer that is an oligonucleotide can have hundreds and even thousands of residues. Similarly, a protein will generally have one hundred or more residues (though the sequencing of smaller fragments, e.g., peptides, is also useful). An oligosaccharide will typically have from 3 to 100 sugar residues. A lipid will normally have 2 or 3 fatty acid residues.

As evidenced above, the term "oligomer" is essentially without bounds, and fairly reads on intact chromosomes as well as unlimited length to polymers, or copolymers such as nylon, which can fairly be measured in terms of miles in length. In view of the term being essentially without limits, the metes and bound of said claims cannot be readily determined.

8. Clams 1-58 are indefinite with what constitutes "a terminal portion."

9. Claims 1-58 are indefinite as a result of defining the mass defect labeling moiety, "first labeling moiety," "labeling moieties" as being "one element with an atomic number from 17 to 77, with the proviso that said element is other than sulfur or phosphorus." It is noted that phosphorus and sulfur have atomic numbers 15 and 16, respectively, and would otherwise fall outside of the range of elements that have an atomic number of from 17 to 77. If in fact S and P would somehow be included within the range of elements that have an atomic number from 17 to 77, the metes and bound of the recited range cannot be determined.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

12. For convenience, claim 1 is reproduced below.

1. (Currently Amended) A method for sequencing a terminal portion of an oligomer, comprising:

(a) contacting said oligomer with a mass defect labeling moiety to covalently attach a the mass defect labeling moiety ~~label~~ to the a terminus of the oligomer and form a labeled oligomer, said mass defect labeling moiety comprising at least one element having an atomic number from 17 to 77, with the proviso that said element is other than sulfur or phosphorus;

(b) fragmenting said labeled oligomer using an enzymatic, chemolytic or mass spectrometric fragmentation method to produce labeled oligomer fragments; ~~and~~

(c) identifying a mass spectrum data corresponding to said labeled oligomer fragments; and

(d) determining the sequence of at least two terminal residues of said labeled oligomer, wherein said sequence determination step ~~comprising identifying a mass spectrum data corresponding to said labeled oligomer fragment or a mass spectrum fragment thereof, wherein said identification step~~ is based at least in part on the mass defect ~~of at least a portion~~ of said labeling moiety, wherein said mass defect is less than 1 amu.

13. For purposes of examination, the claimed method has been interpreted as encompassing the sequencing of any number of polymers in a simultaneous manner, including performing said sequencing any length of said oligomers where one has a mixed population of oligomers,

including, but not limited to, sequencing each chromosome of any cell from an organism as well as any other oligomer associated therewith, e.g., lipids, saccharides (e.g., cellulose), nylon associated with clothing (e.g., fabric collected as part of a crime scene investigation).

14. A review of the specification finds the following examples:

Example 1

In this example, a high mannose-type oligosaccharide (Figure 7) is labeled and sequenced. The oligosaccharide is labeled using methods similar to those described in Parekh, et al., U.S. Patent No. 5,667,984. Briefly, a mass defect label (2-amino-6-iodo-

Example 2

In this example a mass defect label is used for the identification of the fatty acid composition and arrangement in lipids, or "lipid sequencing." This example utilizes

Example 3

This example describes the preparation of photocleavable mass defect labels having bromine or iodine substituents. These labels are useful for quantifying the relative

Example 4

This example illustrates the use of affinity-coupled mass labels for the rapid and quantitative analysis of affinity purified mass defect labeled compounds obtained from different samples. In this example, proteins are used, but one of skill in the art will appreciate

Example 5

This example illustrates the use of photocleavable mass tags in sequencing methods.

Example 6

This example illustrates the use of a photocleavable mass defect label generated in Example 5, above, in sequence determination of bradykinin.

Example 7

This example illustrates the conjugation of a mass-defect label, the N-hydroxysuccinimide (NHS) ester of 5-bromonicotinic acid, to horse apomyoglobin (Myo).

Example 8

This example illustrates the generation of sequencing mass spectral fragment ion species from 5-BrNA labeled myoglobin (prepared as described in Example 7) by IMLS that are shifted from the periodic chemical noise.

Example 9

This example illustrates the conjugation of a mass-defect label, the N-hydroxysuccinimide (NHS) ester of 5-bromo-3-pyridylacetic acid (5-Br-3-PAA), to horse apomyoglobin (Myo).

Example 10

This example illustrates the generation of sequencing mass defect spectral fragment ion species from 5-Br-3-PAA labeled myoglobin (prepared in Example 9) by IMLS that are shifted from the periodic chemical noise.

Example 11

This example describes one method for the IMLS of apomyoglobin labeled with 4-bromobenzaldehyde.

Example 12

This example illustrates the IMLS of ubiquitin labeled with 5-bromonicotinic acid.

Example 13

This example illustrates the IMLS of Apomyoglobin labeled with 6-Bromo-2-hydroxy-quinoline-4-carboxylic acid (BHQC)

Example 14

This example illustrates the IMLS of ubiquitin labeled with 6-bromo-2-hydroxy-quinoline-4-carboxylic acid (BHQC).

Example 15

This example illustrates the use of the automated deconvolution and sequencing algorithms of this invention to find the N-terminal sequence of 5-Br-3-PAA-labeled myoglobin fragmented in-source in an ESI-TOF mass spectrometer as described in Example 5.

Example 16

This example illustrates the synthesis of a generic mass-defect label that incorporates a mass-defect element of this invention (i.e., bromine), an ionizable group (i.e., pyridyl) and a succinic anhydride linking moiety for attachment to the N-terminus or other desired primary or secondary amino group of a polypeptide or other species. It has been

Example 17

This example illustrates the use of mass defect labels in DNA sequencing applications. The scheme presented (Figure 19) represents an exemplary sequencing

Example 18

In this example we use the mass defect label (5-Br-3-PAA) to sequence bovine ubiquitin (Sigma-Aldrich). Ubiquitin was labeled by the same procedure described in

15. As seen above, and by further review of the examples as set forth in the specification, the examples do not provide an adequate written description of methods where polymers of virtually length and composition can be accurately and reproducibly sequenced. The methods clearly do not demonstrate that applicant was in possession of such a board method.

16. As evidenced above, the term "oligomer" has been interpreted as encompassing polymers of virtually any length. The claimed methods fairly encompass the sequencing of such polymers, however, general intimations as to how the claimed method could be broadly applied does not in and of itself raise to the level of constituting an adequate written description of same. While the disclosure has been found to make reference to various documents, said documents have not been properly incorporated by reference and as such cannot now be relied upon for satisfaction of the written description or enablement or bet mode) requirements of 35 USC 112, first paragraph. Therefore, and in the absence of convincing evidence to the contrary, claims 1-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

17. Claims 1-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

It is well settled that one cannot enable that which they do not yet possess. As shown above, the specification fails to provide an adequate written description of the claimed invention and in so doing, fails to reasonably suggest that applicant was in possession of the invention at the time of filing. Accordingly, the specification cannot now enable the same claims.

18. As presented above, the claimed method has been interpreted as encompassing the sequencing of any number of polymers in a simultaneous manner, including sequencing any length of said oligomers where one has a mixed population of oligomers, including, but not limited to, sequencing each chromosome of any cell from an organism as well as any other oligomer associated therewith, e.g., lipids, saccharides (e.g., cellulose), nylon associated with clothing (e.g., fabric collected as part of a crime scene investigation).

19. The specification has been found to contain several examples, however, the examples fail to enable the full scope f the claimed invention. Therefore, and in the absence of convincing evidence to the contrary, 1-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
16 August 2003